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CONTENTS

Click on title to link directly to article.

RESEARCH

	Page
<u>Lung Inflammation Correlated with PM Exposure in Humans.</u>	
<u>Ecological Effects Database Available on the Internet</u>	
<u>Field Tests Held on Ocean Response Coastal Analysis System</u>	
<u>Mechanisms Probed for How Dioxin Causes Birth Defects in Mice</u>	
<u>Stream Conditions Assessed by Sampling Biology</u>	
<u>Toxicity Studies on Brominated Flame Retardants Under Way.</u>	

PUBLICATIONS

<u>Proceedings Issued on Risk Assessment Indicators.</u>	
<u>Booklet on Ecological History of New Bedford Harbor Published . . .</u>	
<u>Proceedings Issued on Microbes and Disinfection By-products in Drinking Water.</u>	
<u>New England Climate Change Report Published</u>	

MEETINGS / CONFERENCES

<u>International Symposium on Polycyclic Aromatic Compounds Held.</u>	
<u>International Breast Cancer Meeting Held</u>	

RESEARCH

Lung Inflammation Correlated with PM Exposure in Humans

A clinical study has found that lung inflammation in humans from exposure to particulate matter (PM) can be associated with increases in hospitalizations and respiratory illnesses observed in epidemiology studies. The study is the first to demonstrate such a correlation and has been reported in the August 15, 2001, issue of *American Journal of Respiratory and Critical Care Medicine* by Drs. Andrew Ghio and Robert Devlin of NHEERL's Human Studies Division. The controlled-exposure study of healthy young adult volunteers is described in an article entitled "Inflammatory Lung Injury after Bronchial Instillation of Air Pollution Particles."

During the 1980s, the Utah Valley near Provo had high PM levels, with the principal point source being a steel mill. While operational, the mill contributed more than 80 percent of industrially related PM in the Valley. When the mill shut down for 13 consecutive months in 1986 and 1987 due to a labor dispute, there was a substantial reduction of PM levels and a statistically significant decrease in health-related measures, including elementary school absences; hospital admissions for bronchitis and asthma in preschool-age children; total hospital admissions for pneumonia, pleurisy, bronchitis, and asthma; pulmonary function abnormalities; and age-adjusted death rates for malignant and nonmalignant respiratory disease.

The availability of PM samples collected before and during mill closure and after its reopening provided a unique opportunity to examine more closely the relationship between PM exposure and respiratory effects in humans. Prior to conducting human exposure studies, Drs. Daniel Costa and Janice Dye of NHEERL's Experimental Toxicology Division, in collaboration with HSD scientists, studied the effects of Utah Valley PM on cultured cells and animals to provide direction in the design of the human study.

The human study found that exposure to extracts of PM samples collected whenever the mill was in operation produced inflammatory changes in the lung similar to those found in a very mild viral infection. Exposure to PM extracts taken during mill closure produced no inflammation. This study also suggests that equal amounts of PM extracts can induce disparate lung injuries. Research is continuing to better understand the specific characteristics of particulate matter that may be eliciting these adverse health effects.

Ecological Effects Database Available on the Internet

NHEERL's Mid-Continent Ecology Division (MED) has updated a toxicity database on the Internet at the EPA ECOTOX(icology) Web site,

<http://www.epa.gov/ecotox> that provides quantitative data on chemical exposures. This expanded version of the database on ecological effects of chemicals improves accessibility for the general public, scientists, and risk assessors studying hazardous pollutants.

ECOTOX includes independently compiled data sets from MED, the EPA Office of Pesticide Programs, Russia, and countries belonging to the Organization for Economic Cooperation and Development. The primary data source, however, is the open, peer-reviewed literature, with test results identified through comprehensive searches, manual data abstraction, and entry of relevant data into the database.

Currently, ECOTOX includes more than 320,000 individual effect records abstracted from 17,195 peer-reviewed publications representing more than 7,800 chemicals and 5,300 aquatic and terrestrial species. The database is updated quarterly.

The majority of all papers published on ecotoxicology since 1986 have been indexed. The current priority is to cover both aquatic and terrestrial articles in the open literature from 1989 to the present, although there are some references to papers published as early as the 1920s. Currently, ECOTOX includes data only on exposure to single chemicals, not mixtures.

ECOTOX has two search modes. Quick Search allows searches by the most commonly requested parameters: major taxonomic classifications, scientific and common species names, general media classification (terrestrial, aquatic), Chemical Abstract Services Registry Number, chemical name, observed effect, and publication year. Advanced Search uses 10 additional search parameters and allows modifications in display formats. Data can be downloaded in either tabular report or ASCII format, with bibliographic citations provided for all data records. The complete ECOTOX database as an ASCII format is available at http://www.epa.gov/ecotox/help/ecotox_download.htm.

Currently, ECOTOX data are not evaluated as to the quality of the test results. By June 2002 the ECOTOX Web site will be linked to an evaluated terrestrial data set being developed at MED with funding from the EPA Office of Solid Waste and Emergency Response. The linkage will have several advantages. Risk-based criteria can be developed for soil contamination of terrestrial plants and animals at hazardous waste sites. Various stakeholders will not need to perform repetitious literature searches and evaluations of toxicity data for the same contaminants at every site, and more consistency among risk analyses will be attained.

Field Tests Held on Ocean Response Coastal Analysis System

Adverse impacts of algal blooms and hypoxia (low dissolved oxygen) in coastal waters have led to environmental problems such as fish kills, shellfish poisoning, and beach closures. An early warning system would allow better planning to prevent or mitigate these environmental impacts. Imagine accessing a Web site that can give both real-time information and forecasts of harmful algal blooms and hypoxia in coastal waters. Such an early warning system is being developed through an Interagency Agreement between NHEERL's Gulf Ecology Division (GED) and the Office of Naval Research, along with research by the National Oceanographic Partnership Program and assistance from other federal agencies, universities, and private companies.

To address environmental issues for the EPA and Navy, the new Ocean Response Coastal Analysis System (ORCAS), is being designed to provide real-time, high-resolution monitoring of multiple biological, physical, chemical, and optical properties in coastal waters. The system uses an array of sensors called profilers that are moored to the ocean floor and programmed to float up a guide wire to the surface while collecting data and transmitting that data to a ship- or shore-based computer.

For more than two weeks in September, 2001, partner scientists and engineers visited GED's research facilities in Gulf Breeze, Florida, for the first field tests of the ORCAS sensors. Conducted aboard a University of Texas research vessel in Pensacola Bay and the Gulf of Mexico, the tests covered deployment and recovery of the sensors, instrument performance, data communication links, data storage, and visualization systems. The initial field test was successful and a more comprehensive field demonstration will be conducted in May 2002 to test the new monitoring system.

Mechanisms Probed for How Dioxin Causes Birth Defects in Mice

Recent research published in the July, 2001, issue of the journal *Toxicological Sciences* provides new insight into the molecular and cellular mechanisms by which 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) produces birth defects when administered to pregnant mice. Conducted by Dr. Lamont Bryant of the School of Public Health at the University of North Carolina at Chapel Hill and supervised by Dr. Barbara Abbott of NHEERL's Reproductive Toxicology Division, this was Bryant's doctoral research project.

Earlier work at NHEERL and elsewhere showed that exposure of pregnant animals to high doses of TCDD, the most toxic of the dioxins, can produce birth defects in the offspring. Among these birth defects in mice are cleft palate and hydronephrosis, a type of kidney damage. TCDD stimulated overgrowth of epithelial cells of the ureter (cells lining the inside of the ureter). The overgrowth blocked the flow of urine to the bladder, resulting in adverse effects on the kidney. An important factor in the

regulation of epithelial cell growth is Epidermal Growth Factor (EGF), which appears to have a role in TCDD-induced cleft palate and hydronephrosis.

Mice that can make EGF are called wild type. Mice were bred in which the genetic capability to produce EGF was removed or “knocked out.” The cells of these mice and their offspring therefore cannot produce EGF. Both wild-type and knock-out mice were treated with TCDD on a specific day of their pregnancies, and their fetal offspring were examined for birth defects. In wild-type mice, where EGF is produced normally, TCDD caused cleft palate. In the TCDD-treated knock-out mice, with no EGF produced, the offspring were resistant to the formation of cleft palate. Although hydronephrosis occurred in both types of mice, the incidence and severity of this defect was increased in the EGF knock-out mice.

These studies show that a cellular factor, EGF, is important in the induction of cleft palate by TCDD. Although EGF is not required for the TCDD-induced production of hydronephrosis, absence of the factor produces an increase of this adverse effect of TCDD on the fetal urinary tract.

Stream Conditions Assessed by Sampling Biology

To determine the condition of aquatic ecosystems, the EPA and its partners need reliable sampling methods that can be applied in a variety of environments. One important aspect of monitoring and describing what is found in streams is the “repeatability” of the sampling results, i.e., whether one gets the same kinds and amounts of fish each time the stream is sampled during any one sampling event. Knowing with accuracy how many and what kinds of fish occur at a site during a particular time is essential for assessing biological integrity, patterns of biodiversity, and the relationships of the fish to the characteristics of their environment. Scientists at the Western Ecology Division (WED) developed and validated a statistical model to quantify the repeatability of sampling methods and published it in the September 2001 issue of *Canadian Journal of Fisheries and Aquatic Sciences*.

Related research involved development of a comprehensive assessment of the stream conditions in the Mid-Atlantic Highlands, an important part of EPA’s Environmental Monitoring and Assessment Program for the Mid-Atlantic states. Scientists at WED and EPA’s National Exposure Research Laboratory developed an index of stream “health” based on descriptions of the fish communities found. Natural differences in fish communities were found, as expected, and were related to stream size, and geographic region in the Mid-Atlantic Highlands. These natural differences were used to adjust the index of “health” so that differences due to natural variability were not confused with differences due to stressors. The relative importance of stressors and natural variability as they affect the current distribution of stream fishes in the Mid-Atlantic Highlands are discussed in the September 2000 issue of the *Journal of*

the North American Benthological Society.

Toxicity Studies on Brominated Flame Retardants Under Way

Scientists at NHEERL's Neurotoxicology and Experimental Toxicology Divisions are studying the potential health effects of polybrominated diphenyl ethers (PBDEs), a class of flame retardants used on commercial products such as electronic equipment and textiles. Although the widespread contamination of ecosystems with these flame retardants is well known, information on their health effects is sparse.

Bioaccumulation of PBDEs, due to long-term persistence in body fat, has led to their detection in humans and wildlife and has become an environmental concern. Recent non-EPA studies have found increases in concentrations of PBDEs in human breast milk and in certain fish.

NHEERL scientists have found that PBDEs are potent endocrine disruptors, affecting circulating levels of thyroid hormones following short-term exposure in the juvenile rat. As published in the January 2001 issue of *Toxicological Sciences*, these chemicals were found to be active at dosage levels in the 3 -10 milligrams per kilogram per day range. Current research is focusing on the effects of PBDEs on thyroid hormones in newborn rats to determine if there are health effects at lower doses of 1 milligram per kilogram per day range. This NHEERL research effort is providing data needed for risk assessments of PBDEs.

PUBLICATIONS

Proceedings Issued on Risk Assessment Indicators

The entire 625-page October, 2001, issue of the *International Journal of Human and Ecological Risk Assessment* covers the proceedings from the 5th NHEERL Symposium, Indicators in Health and Ecological Risk Assessment, held in Research Triangle Park, North Carolina, June 2000. Indicators are measurements used to determine risk and to establish thresholds for management decisions on health and the environment. The symposium goals were to substantiate or improve existing indicators and to integrate human health and ecological issues.

Dr. William Fisher of NHEERL's Gulf Ecology Division (GED) chaired the symposium and served as guest editor of the proceedings. The following list, by name, division, and session title, shows other NHEERL scientists who served as session chairs and editors: Dr. Ralph Cooper, Reproductive Toxicology Division, endocrine disrupting chemicals; Dr. William Mundy and Dr. Stan Barone, Jr., Neurotoxicology Division (NTD), persistent bioaccumulating toxicants; Dr. Michael Madden, Human

Studies Division, ambient ozone; Dr. Henry Walker, Atlantic Ecology Division (AED), global atmospheric change; Drs. Richard Greene, GED, and Kenneth Hudnell, NTD, harmful algal blooms; and Dr. John Paul, AED, coastal communities.

Like the symposium, the proceedings attempt to reconcile the sometimes conflicting views of scientists, risk assessors, and resource and public health managers. Articles by 41 national and international experts examine the development and application of health and ecological indicators for risk in the areas covered in the six sessions. Throughout, the articles address indicator measurements, assessment questions and endpoints, and social values. The results support the role of NHEERL and ORD in promoting sound science in risk assessment.

Booklet on Ecological History of New Bedford Harbor Published

A recent 32-page booklet *"Imprint of the Past: Ecological History of New Bedford Harbor"* (U.S. EPA, Region 1; 2001; No. 901-R-01-003), has been produced by NHEERL's Atlantic Ecology Division, the New Bedford Whaling Museum in Massachusetts and EPA Region 1 Office in Boston for the general public and teachers. It is available at <http://www.epa.gov/nbh>, the new public Web site.

In addition to describing New Bedford Harbor's ecological history, the booklet includes a general section on environmental contaminants, a glossary, maps and figures, a listing of relevant organizations in New Bedford, and old photographs, prints, and paintings from the New Bedford Whaling Museum.

Ecological history, the study of the interaction between humans and their environment, is especially relevant in New Bedford Harbor, Massachusetts. Although New Bedford Harbor gained notoriety in 1982 when it was named a Superfund site because of its PCB contamination in sediments, the current environmental conditions are the result of more than 250 years of agricultural, commercial, and industrial activity.

The development of ecological histories is relevant to EPA because they are useful tools in community-based environmental protection and they promote the involvement of the local citizens. They also provide managers with realistic goals for remediation or restoration, give scientists a more complete understanding of current conditions, and educate business leaders and citizens.

Other products from this study include two journal articles: "Historical Analysis, A Valuable Tool in Community-based Environmental Protection" in the May 2001 issue of *Marine Pollution Bulletin* uses New Bedford Harbor as a case study to explain the value of ecological histories to managers and scientists. "A Story of Urbanization and Ecological Connections" in the July 2000 issue of *Environmental History* documents the New Bedford story for environmental historians.

Proceedings Issued on Microbes and Disinfection By-products in Drinking Water

Although chlorine has long been the standard treatment for removing microbial contamination from public drinking water supplies, there is growing concern about balancing the need to remove microorganisms from water by disinfection and the toxicity of certain disinfection by-products (DBPs). What other methods of disinfection are available? What are their relative risks, benefits, and costs? Do developed and developing countries have the same concerns? Eight NHEERL scientists are among the contributors to a 656-page proceedings from an international conference that addresses these and other questions. Dr. Fred Hauchman served as a contributor and editor. NHEERL was also one of 11 co-sponsors of the conference and publication.

The published proceedings entitled “Microbial Pathogens and Disinfection By-products in Drinking Water: Health Effects and Management of Risks” are from the Second International Conference on the Safety of Water Disinfection: Balancing Chemical and Microbial Risks, held in Miami Beach, Florida, Nov. 15-17, 1999. Almost 200 scientists, drinking water investigators, and regulators from 31 countries attended the conference.

Key features of both the conference and the proceedings were interdisciplinary participation, a global scope of both the presentations and participants, evaluation of needs and priorities in developed versus developing countries, and the effects of regional and geographic differences on decision-making related to ensuring the safety of drinking water supplies.

Increases in population size and associated stresses continue to limit the availability of clean water in many areas of the world. The proceedings provide a current picture of the available information related to water disinfections and indicates the direction of future priorities. The paperback publication, ISBN 1-57881-117-1, issued August 21, 2001, is available from ILSI Press, Washington, DC.

New England Climate Change Report Published

Dr. Henry Walker at NHEERL's Atlantic Ecology Division co-authored two chapters of an 88-page report on *Preparing for a Changing Climate. The Potential Consequences of Climate Variability and Change: New England Overview*, published in September by the University of New Hampshire.

Global warming during the 20th century is shown to be associated with significant environmental changes in New England, including milder winters, reduced snowfall, earlier ice-thawing in lakes during the spring, earlier maple-sap flow, and a decrease in selected fish populations. Over the past 100 years, there has been a long-term trend in decreased maple sap and syrup production in New England and, in

the last 30 years, a major increase in their production in Canada. Winter flounder, a major, commercially important flatfish, breeds and lays eggs on the bottom in cold, shallow estuarine waters in mid-winter when predation rates are low. Between 1960 and 1990, when the winter water temperature of Narragansett Bay increased by almost 5 degrees Fahrenheit, the abundance of flounder declined rapidly.

Two climate prediction models used in this study were based on a scenario of global atmospheric carbon dioxide levels increasing at a rate of about one percent of 1990 levels per year over the next century. As a result, the models projected a 6 to 10 degree Fahrenheit increase in New England's temperatures by 2100. That high of an increase could result in the climate of Boston becoming more like that of Richmond, Virginia, or Atlanta, Georgia. Under the simulated 2100 climate, the dominant New England forest cover eventually could change from spruce/fir and maple/beech/birch to one of oak/pine/hickory. There could also be a 50-100 percent loss of habitat favorable for brown, brook, and rainbow trout, cold freshwater fish highly valued for sport fishing. Continued warming of saltwater could also reduce the food supply to bottom-dwelling species, with adverse impacts on important commercial fisheries.

Funding for this New England Regional Assessment (NERA) was provided by the National Science Foundation as part of the U.S. Global Change Research Program. A direct link to the report is at <http://www.necci.sr.unh.edu/2001-NERA-report.html>. Paper copies are available by contacting the University of New Hampshire at 603-862-1792.

MEETINGS / CONFERENCES

International Symposium on Polycyclic Aromatic Compounds Held

Polycyclic aromatic compounds (PACs) are among the oldest known human carcinogens, and because of their human and ecological exposure, pervasiveness, and abundance, this class of compounds has been widely studied. NHEERL and EPA's Office of Solid Waste and Emergency Response were two of 10 co-sponsors of the 18th International Symposium on Polycyclic Aromatic Compounds, held Sept. 9-13, 2001, at the University of Cincinnati. Drs. Stephen Nesnow and Jeffrey Ross of the NHEERL Environmental Carcinogenesis Division (ECD) co-chaired the program committee and, with Dr. James Rabinowitz of ECD, also chaired scientific sessions.

The 177 attendees from 14 nations focused on recent scientific developments in the chemistry and biology of PACs and related compounds and identified important advances, areas for research, and themes for multi-disciplinary collaboration. Session topics included the molecular biology of PAC carcinogenesis; human and environmental exposure; chemical analysis and synthesis; environmental aspects such as biodegradation, bioremediation, and ecotoxicology; and risk assessment.

The symposium also included six short courses on the chemistry and detection of PACs and metabolites in environmental and biological samples, and the biology and molecular epidemiology of PACs, as well as exhibits from suppliers and manufacturers. The proceedings will be published in the journal *Polycyclic Aromatic Compounds* in 2002.

International Breast Cancer Meeting Held

An international meeting on the environmental factors associated with breast cancer was held Sept. 22-25, 2001, in Research Triangle Park (RTP), North Carolina. Co-sponsors were NHEERL, National Institute of Environmental Health Sciences, National Cancer Institute, Genentech, and the local chapter of the Environmental Mutagen Society (EMS), the Genotoxicity and Environmental Mutagen Society.

Dr. David DeMarini of NHEERL's Environmental Carcinogenesis Division and president of EMS, chaired the meeting. More than 100 scientists, physicians, and students attended to hear 27 invited speakers from around the world. Only five speakers and eight pre-registered attendees were unable to come to RTP because of the events of September 11.

There were sessions on the epidemiology of breast cancer; general trends from animal studies; environmental mutagens/carcinogens, including carcinogens in food, tobacco, and industrial sources as potential causes of the cancer; and the mechanisms of breast cancer formation. Workshops were conducted by breast cancer survivors and by members of the National Breast Cancer Coalition, a group active in prevention and support activities.

Concluding sessions covered the genetics of breast cancer and promising new treatments for this disease. Taxol, one of the main drugs used to treat breast cancer, was discovered by Drs. Monroe Wall and M.C. Wani of the Research Triangle Institute, Research Triangle Park, North Carolina. Wani concluded the meeting with an overview of their discovery and development of this drug.